

Animal Nutrition

Meat diets and fragile bones: Inferences about osteoporosis¹

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Abstract

Because women supplemented with copper have improved bone density and femurs of rats deficient in copper have decreased mechanical strength, the hypothesis that mice fed meat would have fragile bones was tested. Mice fed sirloin are hypercholesterolemic in comparison to mice fed meat and beef liver because of a relative deficiency of copper compared to zinc. Male, albino, Swiss mice were fed trimmed sirloin or sirloin supplemented with beef liver (3/1 by weight). After 62 days, when hypercholesterolemia was detected, mice were killed and femurs were removed, cleaned and dried. Breaking strength was measured carefully at room temperature. The meat diet produced femurs 23% weaker (8.8 ± 0.70 N/mg·100 vs 11.4 ± 0.92 , $\bar{x} \pm SE$, $p < 0.04$) in comparison to meat plus liver. Calcium, copper and phosphorus concentrations were unaffected but zinc was mildly elevated in the weak bones (426 ± 17.5 µg/g vs 355 ± 9.23 , $p < 0.002$). These elements generally are unaltered in osteoporotic bones. Because copper deficiency produces osteoporosis in animals and people and because the Western diet often is low in copper, further tests of the hypothesis that diets low in copper contribute to osteoporosis are warranted.

Key words: bone mineral, calcium, copper deficiency, osteoporosis, Western diet

Introduction

Hegsted (1) suggested that osteoporosis is largely a disease of affluent, western⁴ cultures and noticed that hip fractures increased along with per capita protein consumption upon examining data collected from 10 nations. He also suggested that some of these diets are sufficient-

ly high in protein that advice to increase consumption of dairy products probably should be accompanied by advice to decrease meat consumption. Walker et al. (2) also infer that a lower intake of protein may be protective. Burkitt included osteoporosis among the diseases associated with

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the Western⁴ diet (3). Strain (4) reviewed epidemiologic and experimental data and suggested that osteoporosis is largely a disease of affluent, western⁴ cultures.

Although the harmful effects of meat diets on bone have been known for more than a century, research has been infrequent. Moore and Sharmen quoted Röhl's textbook of 1860 on rickets in young leopards (5) and observations of Bland Sutton three decades later on deformities in lion cubs at the London Zoo. Both the leopards and lions were spared deformity if allowed to eat bone along with meat. When young rats were fed lean beef supplemented with calcium carbonate, growth was rapid and radiography improved in comparison to unsupplemented rats (5). These authors inferred meat is deficient in calcium and did not mention anemia.

Research emphasis then shifted from the skeleton to hematology. Mice fed only beef muscle developed severe anemia. In a series of experiments, skeletal muscle of beef induced more severe anemia than muscle from other species, and beef liver (at the 25% level) was the best anemia preventive (6). Later, supplementation with copper sulfate was found to be curative (7). Guggenheim later concluded that meat anemia is due to "... insufficient amounts of copper accompanied by an excess of zinc," whose "effects are accentuated by a concomitant lack of calcium" (6, 8). Calcium supplementation lessens the adverse effect of too much zinc.

After hypercholesterolemia was produced in rats by a high ratio of zinc to copper (9), meat anemia was produced in mice by the original method to look for hypercholesterolemia. Hematocrits decreased by 56% and plasma cholesterol increased by 26% with the meat diet (10).

Availability of femurs saved from this experiment permits their evaluation. As femurs from rats deficient in copper have decreased mechanical strength (11, 12), it was decided to test the hypothesis that those from the mice would be similarly weak.

Materials and Methods

In brief, male, albino, Swiss mice were divided into two groups matched by mean weight at three weeks of age and were housed in small groups in cages free of nutritionally available trace elements (10). One group received beef sirloin which had been trimmed free of fat and connective tissue; the other group received three parts sirloin to one part beef liver by weight. Animals were killed after 62 days; femurs were removed, scraped clean of muscle and were stored in small plastic vials at room temperature. Bones were sent to Newark, DE⁵ for breaking strength measurements; fragments were sent back to Grand Forks for dissolution in nitric acid and hydrogen peroxide for measurement of metallic elements by inductively coupled plasma spectrometry (13). Femurs were dried at 37 °C in

an oven to constant weight and were placed within the grip of an Instron (Model 1322, Instron Corp., Dayton OH). Breaking strength was determined (12) at room temperature. The bone had a force applied to it at a displacement rate of 200 mm/min. Every 0.2 sec the force applied was recorded. Force strain curves were obtained and the point of rapid decrease in force was used as the point of the fracture force and recorded. Data were analyzed by the "t" test corrected for unequal variances (14).

Results

Data on hematocrits and cholesterol (taken from (10)) are included in Table 1 along with peak breaking strength of femurs to verify that meat anemia had been produced. Femurs from mice fed only meat were on the average 23% weaker ($p < 0.04$) than those from mice fed meat plus liver. The only significant difference in metallic elements in femurs was an increase in zinc in mice fed meat (Table 2).

Discussion

Data in Table 1 integrate three phases of research on effects of diets high in meat. This experiment demonstrates anemia, hypercholesterolemia and bone fragility in mice. Copper in the diet (12 µg/g) with liver probably was the ingredient that improved the strength of the bones of mice fed meat (0.75 µg/g) (10). Chemical data in Table 2 generally are consonant with data of others in similar experiments. Taken together, they may explain the plight of the leopards and lions in London (above). The hypothesis that the bones from mice fed meat would be weak was tested successfully.

Other Experiments with Animals

Ilan et al. (15) showed that an all meat diet supplemented with calcium, copper, liver or manganese produced an increase in bone ash of mice. Calcium produced the largest benefit of the several supplements. No individual elements were measured in bone.

Guggenheim et al. (16) found that copper supplementation of diets only of meat increased bone ash, calcium and phosphorus in fresh bone, in contrast to the data in Table 2. Effects were variable depending on the size of the copper supplement and the length of the experiment. Ulmansky (17) found that copper mitigated the osteoporotic histology of mice fed meat, but calcium was less effective.

Baxter and Van Wyk (18) found diffuse osteoporosis in dogs deficient in copper, two thirds of which were either lame or had leg deformities and one third of which had fractures. Calcium, phosphorus and Ca:P ratios were quite similar in comparison to dogs supplemented with copper (19). Jonas et al. (11) found that copper deficiency did not decrease the ash weight or calcium content of the fragile bones of rats. Medeiros et al. (12) extended these observations and found that copper deficiency had no effect on the calcium, phosphorus or zinc concentrations or on the Ca:P ratio; bone copper was decreased, however.

⁴ Not all authors capitalize the word Western in this context; we prefer Burkitt's style.

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Table 1. Hematology and Peak Breaking Strength, mean \pm SE

	Hematocrit (%)	Cholesterol (mg/dL)	Strength (N/mg \cdot 100)*
Meat (n= 22)	24.5 \pm 2.3	121 \pm 7.5	8.8 \pm 0.70
Meat + liver (n= 30)	55.4 \pm 1.3	96 \pm 4.7	11.4 \pm 0.92
P	< 0.001	< 0.01	< 0.04

*n = 17, 25; N = Newton, or 1 kg $\cdot \frac{1\text{m}}{\text{sec}^2}$

Table 2. Chemical Analyses of Bone, mean \pm SE

	Calcium (mg/g)	Phosphorus (mg/g)	Copper ($\mu\text{g/g}$)	Zinc ($\mu\text{g/g}$)
Meat (n= 17)	98.3 \pm 2.5	48.0 \pm 1.14	2.80 \pm 0.36	426 \pm 17.5
Meat + liver (n= 28)	105.7 \pm 2.7	50.9 \pm 1.22	2.85 \pm 0.18	355 \pm 9.23
P	>0.05	>0.09	>0.9	< 0.002

Osteoporosis – Radiology and Chemistry

In the industrialized world, osteoporosis is the most common metabolic bone disease (20). Osteoporosis often is defined statistically as a reduction in bone mass detected by radiologists who evaluate bone mineral density by various methods (20, 21) that measure the ability of a volume of bone to attenuate x-rays of various energies. This attenuation is attributed to an area of bone in two dimensions much like an image on a standard x-ray film. Likelihood of fracture is directly related to bone mass determined in this way (20). The terms bone mass and bone mineral density seem interchangeable (20). Biochemical measurements in osteoporosis usually are normal and serve to exclude other diseases such as Paget's disease, hyperparathyroidism or homocystinuria. Bone biopsy is neither useful nor necessary (20).

Surprisingly little seems to have been written about calcium, phosphorus and trace elements in human bone. Articles mentioning bone minerals often are about radiology, not chemistry. Driessens and Verbeeck (22) provide no comparisons between the chemistry of normal and osteoporotic bone.

Gron et al. (23) claimed no difference in calcium or phosphorus between osteoporotic and normal bone, but the source of the normal values used in comparison was obscure. Uotila and Visapää (24) confirmed this work with a few samples and also found no difference in Ca:P ratio. Mueller et al. (25) concluded that the amount of ash from bone is normal in osteoporosis, but marrow spaces were larger, so that ash per unit volume of bone was decreased. The Birkenhägers (26) also found little change in calcium, phosphorus, or calcium-phosphorus ratio in osteoporosis. These results are in contrast to those of Burnell (27) who found significantly less calcium and phosphorus in osteoporotic bone without a change in Ca:P ratio. Others have included some trace elements among those measured in bone. No remarkable difference was found between normal and osteoporotic bone in calcium, phosphorus, copper or zinc by Lappalainen et al. (28). Baslé et al. (29) confirmed these latter results and also found no differences in Ca:P ratio.

There is an apparent incongruity between bone chemistry and bone radiology in osteoporosis. Overall there seems to be little change in calcium, phosphorus or Ca:P ratio in osteoporotic bone. Chemical data summarized above generally are based on concentrations. The data of Mueller et al. (25) on less ash per unit of volume of bone in osteoporosis reconciles the chemistry with the radiology because Smith (20) states that osteoporosis is a reduction in the amount of bone per unit volume. In addition, thirty-one vertebrae were removed from 11 fresh cadavers, scanned by dual energy absorptiometry, and converted to ash; radiologic measurement and ash were correlated (30). A single reference correlated radiologic measurements on six fetal human femurs with both ash and calcium (31). Limited data from animals also reveal a correlation between radiologic measurement and bone ash (32–36). Plain films of the skeleton do not detect osteoporosis (20) until there is considerable loss of bone. Perhaps bone biopsies should be used more frequently so that pathology can be defined better.

Osteoporosis – Etiology

The dietary conditions implied by Hegsted (1), Burkitt (3) and Walker et al. (2) probably produce their adverse effects on bone over many years, perhaps decades. There is a wide-spread belief that extra dietary calcium is ben-

Table 3. Similarities between animals deficient in copper and osteoporosis in people

Generally normal:	Decreased:
calcium, phosphorus and Ca:P ratio of bone	attenuation of x-ray bone strength osteoblast activity serum copper
Mitigated by: calcium supplements copper supplements	

eficial to osteoporosis. In spite of important limitations in the evidence, considerations about bone health are very prominent in estimating human requirements for calcium (21) because extra calcium sometimes seems to improve osteoporotic bone. Short term dietary experiments, with protein or proteinaceous foods may not be useful in determining whether or not protein is responsible for the osteoporosis associated with affluence or in defining the effective dose even though they seem (37) capable of producing a daily loss of calcium of approximately 30 mg.

This amount of calcium loss seems capable of producing osteoporosis over adulthood if no adaptation occurs. Its smallness in comparison to many daily intakes (less than 5%) may prevent correct interpretation of data germane to a life-long illness. Whether or not the amount of protein in the Western diet is sufficient to explain the association between this diet and a high prevalence of osteoporosis is unknown.

Perhaps a more subtle characteristic of the Western diet has a greater influence on bone health than the protein. The Western diet which is high in energy, sugars and fat, in addition to protein, also seems to be low in copper (38, 39). In brief, approximately one third of 849 representative daily diets made of conventional foods in Belgium, Canada, the U.K. and U.S. contain less than 1 mg of copper. Diets such as these have been proved insufficient for more than 30 men and women in controlled, clinical trials (39, 40).

Strain (4) suggested that copper may be a limiting nutrient in many western⁴ diets and hypothesized that mild dietary copper deficiency may be implicated in the onset and progression of osteoporosis. He emphasized the low amount of copper in milk and the possible interference of lactose with copper metabolism as being more important than effects of other minerals. Cordano et al. (41, 42) were first to demonstrate that copper deficiency in people is characterized by, *inter alia*, osteoporosis. Numerous other observations, mostly on children, are consonant (43–57). Osteoporosis detected in these cases by standard x-ray films is much more severe than that detected from more sensitive methods such as dual x-ray absorptiometry because 20 to 40% of bone mass must be lost (58, 59) to be detectable by routine x-rays. Treatment with copper has produced improvement (47, 51, 52) or cure (44, 46, 49, 54, 56, 57) of this osteoporosis. Copper supplements have been found beneficial to osteoporotic women as well (60, 61). Low serum copper in patients with fractures of the femoral neck (62) or decreased lumbar bone density (63) may indicate mild copper deficiency. Carnes (64) suggested that some of the skeletal abnormalities of copper deficiency result from an inadequacy of supporting structure.

There are other similarities (Table 3) between animals with low copper status and people with osteoporosis in addition to the bone fragility and minimal changes in calcium or phosphorus noted above. Extra dietary calcium and extra dietary copper have improved the bones of animals fed meat (5, 16).

The *sine qua non* of osteoporosis seems to be a radiolucency of bone; bones of animals fed meat are radiolucent

(5, 15). Osteoblast activity is decreased in both human osteoporosis (65–68) and copper deficiency (17, 19, 69).

In summary, diets high in meat have produced poor quality bone in a variety of animal species. A substantial amount of this pathology is the result of an insufficient amount of dietary copper. Although human diets associated with high rates of osteoporosis are high in protein, they also seem to be low in copper. The minimal amount of protein needed to produce skeletal pathology over the long term is unknown; extra dietary copper may be protective, however. People deficient in copper have osteoporosis; chemical, physiological and radiological similarities between animals deficient in copper and people with osteoporosis have been identified. Further tests of the hypothesis that diets low in copper contribute to human osteoporosis are warranted.

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